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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,396	08/30/2001	Kevin P. Baker	P2548P1C11	2338

28442 7590 09/26/2002

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EXAMINER
KEMMERER, ELIZABETH

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/944,396	Applicant(s) BAKER ET AL.	
	Examiner Elizabeth C. Kemmerer, Ph.D.	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 22-27 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 22-27 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The sequence listing has been found to be free of errors and has been entered into the file. The preliminary amendments filed 30 August 2201 (Paper Nos. 3 and 4) and 09 September 2002 (Paper No. 7) have been entered in full. Claims 1-21 are canceled. Claims 22-27 are under examination.

35 U.S.C. §§ 101 and 112, First Paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-27 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

The claims are directed to antibodies that bind the PRO357 polypeptide of Figure 26 (SEQ ID NO: 69). The utility of the antibody depends upon the utility of the polypeptide it binds.

The specification teaches that PRO357 has (unspecified) homology to the acid-labile subunit of insulin-like growth factor-1 (ALS), which is a member of the leucine-rich

repeats containing protein family (pp. 6-7). At pp. 6-7, the specification states that leucine rich proteins are known in the art to bind other proteins. However, the proteins that are bound are highly diverse, as are the downstream effects of the binding interactions. The structure of the putative PRO357 peptide is discussed at p. 13-14 of the specification, however there is no disclosure that the protein is expected to be a transmembrane protein, nor of the location of any specific extracellular domain. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner, or any other specific feature that is disclosed as being associated with PRO357. Without any information as to the specific properties of PRO357, the mere identification of such as belonging to the leucine rich protein family is not sufficient to impart any particular utility to the claimed antibodies.

At p. 80, it is stated that PRO357 can be used in competitive binding assays with ALS to determine its activity with respect to ALS. However, there is no disclosure that PRO357 binds ALS or any other specific protein. It is noted that PRO357 and ALS are only about 10% identical over about half the length of the PRO357 protein (see alignment in Attachment A). One skilled in the art would consider this far too low to be predictive of any shared function.

At pp. 125-127, it is disclosed that nucleic acids encoding PRO357 had a ΔCt value of at least 1.0 for a number of primary lung and colon tumors. At page 121, ΔCt is defined as the threshold PCR cycle, or the cycle at which the reporter signal accumulates above the background level of fluorescence. The specification further indicates that ΔCt is used as a quantitative measurement of the relative number of

starting copies of a particular target sequence in a nucleic acid sample when comparing cancer DNA results to normal human DNA results. The Examiner is unable to find, either in the specification or in the art, an explanation of how ΔCt values are calculated, nor what the significance of such are. It is noted that the specification states that samples are used if their values are within 1 Ct of the "normal standard". It is further noted that the ΔCt values are expressed (a) with values to one one-thousandth of a unit (e.g. 1.185), and (b) that only one four samples out of 42 gave values that were consistently (at least on a sample size of 2) at least 2. It is not clear how measurements of hundredths of a PCR cycle can be made, nor what the significance of a difference of 1 or 2 PCR cycles would be. Given the paucity of information, the data do not support the implicit conclusion of the specification that PRO357 shows a positive correlation with lung and colon cancer, much less that the levels of PRO357 would be diagnostic of such. Even *if* the data demonstrated a slight increase in copy number of PRO357 nucleic acids in primary tumors, such would not be indicative of a use of the encoded polypeptide as a diagnostic agent. Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12:82-88). The data presented in the specification were not corrected for aneuploidy. A slight amplification of a gene does not necessarily mean overexpression in a cancer tissue, but can merely be an indication that the cancer tissue is aneuploid. The preliminary data were not supported by analysis of mRNA or protein expression, for example. Thus, the data do not support the implicit assertion that PRO357 can be used as a cancer diagnostic. Significant further research would have been required of the

skilled artisan to determine whether PRO357 is overexpressed in any cancer to the extent that it could be used as a cancer diagnostic, and thus the implicitly asserted utility is not substantial.

Claims 22-27 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22 and 27 differ only with respect to the recitation of "binds" in claim 22 and "specifically binds" in claim 27. Absent a definition in the specification regarding what the difference between the two terms is, one skilled in the art would be unable to determine what the difference in scope between the two claims is. Therefore, the metes and bounds of the two claims cannot be determined.

Priority Determination

As the claimed subject matter is found to lack utility and enablement under 35 U.S.C. §§ 101 and 112, first paragraph, respectively, the effective priority date for this application is the instant filing date, 30 August 2001.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 22-27 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Holtzman (U.S. Patent 6,225,085 B1).

Holtzman discloses a polypeptide, LRSG, which is 98.4% identical to the instant SEQ ID NO: 69 (see SEQ ID NO: 2 of Holtzman, and alignment attached in Attachment B). Holtzman teaches an antibody that binds (or specifically binds) this polypeptide at

column 22, line 24, to top of column 25. Holtzman teaches monoclonal, humanized and labeled antibodies, as well as antibody fragments.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (703) 308-2673. The examiner can normally be reached on Mon. - Thurs., 6:30 to 4:00, and alternate Fri..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elyabeth C. Kemmerer

ECK
September 25, 2002

ELIZABETH KEMMERER
PRIMARY EXAMINER

ATTACHMENT A: ALIGNMENT OF PRO357 (UPPER SEQUENCE) AND ALS (LOWER SEQUENCE)

```
RESULT   1
US-09-063-950-2
; Sequence 2, Application US/09063950C
; Patent No 6225085
; GENERAL INFORMATION:
;  APPLICANT: Holtzman, Douglas A.
;  TITLE OF INVENTION: NOVEL LRSG PROTEIN AND NUCLEIC ACID MOLECULES AND USES
;  TITLE OF INVENTION: THEREFOR
;  FILE REFERENCE: MEI-019
;  CURRENT APPLICATION NUMBER: US/09/063,950C
;  CURRENT FILING DATE: 1998-04-21
;  NUMBER OF SEQ ID NOS: 9
;  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 2
;   LENGTH: 673
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-09-063-950-2

  Query Match             98.4%;  Score 3083.5;  DB 4;  Length 673;
  Best Local Similarity   88.7%;  Pred. No. 9e-214;
  Matches  597;  Conservative    0;  Mismatches    1;  Indels   75;  Gaps    1;

Qy       1 MCSRVPLLLPLLLLLALGPGVQGCPSGCQCSQPQTVFCTARQGTTVPRDVPPDTVGLYVF 60
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MCSRVPLLLPLLLLLALGPGVQGCPSGCQCSQPQTVFCTARQGTTVPRDVPPDTVGLYVF 60

Qy      61 ENGITMLDASSFAGLPGLQLLDLSQNQIAS---------------------------- 90
           ||||||||| ||||||||||||||||||||
Db      61 ENGITMLDAGSFAGLPGLQLLDLSQNQIASLPSGVFQPLANLSNLDLTANRLHEITNETF 120

Qy      91 --------------------------------------------LRLPRLLLLDLSHNS 105
                                                         |||||||||||||||
Db     121 RGLRRLERLYLGKNRIRHIQPGAFDTLDRLLELKLQDNELRALPPLRLPRLLLLDLSHNS 180

Qy     106 LLALEPGILDTANVEALRLAGLGLQQLDEGLFSRLRNLHDLDVSDNQLERVPPVIRGLRG 165
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 LLALEPGILDTANVEALRLAGLGLQQLDEGLFSRLRNLHDLDVSDNQLERVPPVIRGLRG 240

Qy     166 LTRLRLAGNTRIAQLRPEDLAGLAALQELDVSNLSLQALPGDLSGLFPRLRLLAAARNPF 225
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 LTRLRLAGNTRIAQLRPEDLAGLAALQELDVSNLSLQALPGDLSGLFPRLRLLAAARNPF 300

Qy     226 NCVCPLSWFGPWVRESHVTLASPEETRCHFPPKNAGRLLLELDYADFGCPATTTATVPT 285
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     301 NCVCPLSWFGPWVRESHVTLASPEETRCHFPPKNAGRLLLELDYADFGCPATTTATVPT 360

Qy     286 TRPVVREPTALSSSLAPTWLSPTAPATEAPSPPSTAPPTVGPVPQPQDCPPSTCLNGGTC 345
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     361 TRPVVREPTALSSSLAPTWLSPTAPATEAPSPPSTAPPTVGPVPQPQDCPPSTCLNGGTC 420

Qy     346 HLGTRHHLACLCPEGFTGLYCESQMGQGTRPSPTPVTPRPPRSLTLGIEPVSPTSLRVGL 405
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     421 HLGTRHHLACLCPEGFTGLYCESQMGQGTRPSPTPVTPRPPRSLTLGIEPVSPTSLRVGL 480

Qy     406 QRYLQGSSVQLRSLRLTYRNLSGPDKRLVTLRLPASLAEYTVTQLRPNATYSVCVMPLGP 465
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     481 QRYLQGSSVQLRSLRLTYRNLSGPDKRLVTLRLPASLAEYTVTQLRPNATYSVCVMPLGP 540

Qy     466 GRVPEGEEACGEAHTPPAVHSNHAPVTQAREGNLPLLIAPALAAVLLAALAAVGAAYCVR 525
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     541 GRVPEGEEACGEAHTPPAVHSNHAPVTQAREGNLPLLIAPALAAVLLAALAAVGAAYCVR 600

Qy     526 RGRAMAAAAQDKGQVGPGAGPLELEGVKVPLEPGPKATEGGGEALPSGSECEVPLMGFPG 585
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     601 RGRAMAAAAQDKGQVGPGAGPLELEGVKVPLEPGPKATEGGGEALPSGSECEVPLMGFPG 660

Qy     586 PGLQSPLHAKPYI 598
           |||||||||||||
Db     661 PGLQSPLHAKPYI 673
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ATACHMENT B: ALIGNMENT OF PRO357 (UPPER SEQUENCE) AND SEQ ID NO: 2 OF HOLTZMAN (LOWER SEQUENCE)

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insulin-like growth factor acid-labile chain - baboon
C;Species: Papio sp. (baboon)
C;Date: 17-Apr-1997 #sequence_revision 09-May-1997 #text_change 09-May-1997
C;Accession: JC5239
R;Delhanty, P.; Baxter, R.C.
Biochem. Biophys. Res. Commun. 227, 897-902, 1996
A;Title: The cloning and expression of the baboon acid-labile subunit of the insuli
A;Reference number: JC5239; MUID:97040714
A;Contents: liver
A;Accession: JC5239
A;Molecule type: mRNA
A;Residues: 1-605 <DEL>
C;Comment: This factor is structurally related to proinsulin and have insuline-like

  Query Match           10.3%;  Score 322;  DB 2;  Length 605;
  Best Local Similarity  36.2%;  Pred. No. 1.9e-11;
  Matches  100;  Conservative   39;  Mismatches   97;  Indels   40;  Gaps   11;

Qy       7 LLLPLLLL--LALG--------PGVQG------CPSGCQCSQPQ-----TVFCTARQGTT 45
           | | ||||  :|||         ||  |      ||: | ||         :|||::|  |
Db       8 LALALLLLSWVALGPRSLEGAEPGTPGEAEGPACPATCACSYDDEVNELSVFCSSRNLTR 67

Qy      46 VPRDVPPDTVGLYVFENGITMLDASSFAGLPGLQLLDLSQNQIASLRLPRLLL------- 98
           :|  :|  |  |::  | :: :  ::|  |  |  |:|   |: ||  |: ||
Db      68 LPDGIPGGTQALWLDSNNLSSIPPAAFRNLSSLAFLNLQGGQLGSLE-PQALLGLENLCH 126

Qy      99 LDLSHNSLLALEPGILDTANVEALRLAGLG---LQQLDEGLFSRLRNLHDLDVSDNQLER 155
           | |  | | :|  |    |   || | ||    | :|::|||  | || ||::  | |
Db     127 LHLERNQLRSLAVGTF--AYTPALALLGLSNNRLSRLEDGLFEGLGNLWDLNLGWNSLAV 184

Qy     156 VP-PVIRGLRGLTRLRLAGNTRIAQLRPEDLAGLAALQELDVSNLSLQALPGDLSGLFPR 214
           :|    ||| ||  | |||| |:| |:|   :||| |:|||:|  :|:|:  ::    ||
Db     185 LPDAAFRGLGGLRELVLAGN-RLAYLQPALFSGLAELRELDLSRNALRAIKANVFAQLPR 243

Qy     215 LRLLAAARNPFNCVCPLSWFG----PWVRESHVTLA 246
           |: |   ||    | | :: |     |:  ||  :|
Db     244 LQKLYLDRNLIAAVAPGAFLGLKALRWLDLSHNRVA 279
```